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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,816	04/30/2001	Paul F. Corey	MSE #2609	3320

7590

10/03/2003

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EXAMINER

ZUCKER, PAUL A

ART UNIT

PAPER NUMBER

1621

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/844,816

Applicant(s)

COREY ET AL.

Examiner

Paul A. Zucker

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 11-44 is/are pending in the application.
- 4a) Of the above claim(s) 12-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 11, 42 and 44 is/are rejected.
- 7) ☒ Claim(s) 44 is/are objected to.
- 8) ☒ Claim(s) 1-44 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10. 6) ☐ Other: _____

DETAILED ACTION

Current Status

1. This action is responsive to Applicants' amendment of 21 July 2003 in Paper No 9.
2. Receipt and entry of Applicants' amendment is acknowledged.
3. Applicant's cancellation of claims 6-9 is acknowledged.
4. Claims 1-5, 11, and 42-44 remain pending.
5. The objection to the specification set forth in paragraph 2 of the previous Office Action in Paper No 8 is withdrawn in response to Applicant's amendment.
6. The rejections under 35 USC § 112, second paragraph, set forth in paragraphs 4-5 of the previous Office Action in Paper No 8 are withdrawn in response to Applicant's amendment.
7. The rejection under 35 USC § 102 (b) set forth in paragraph 6 of the previous Office Action in Paper No 8 is withdrawn in response to Applicant's amendment.
8. The rejection under 35 USC § 103 set forth in paragraph 6 of the previous Office Action in Paper No 8 is withdrawn as moot in response to Applicants' comments.

The instantly claimed compounds are neither disclosed nor fairly suggested by the closest art of record: Gray et al (Enzyme Microb. Technol. 1983, 5, pages 137-142) and Aldrich (Aldrich Catalog Handbook of Fine Chemicals, 1994, Milwaukee, WI, page 1020). Applicants have persuasively argued (Amendment, page 10, lines 14-17) that, since Gray teaches that the 2-naphthyl- α -N-benzoyl-N^G-nitroarginate would not be expected to be suitable as a trypsin substrate, one of ordinary skill in the art would not have been motivated to modify the compound of Gray to produce the

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isomeric 2-naphthyl- α -N-benzoyl-N^G-nitroarginate as suggested by Aldrich. The instantly claimed compounds are therefore patentable over the teachings of Gray and Aldrich.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds in which R³ is 1-naphthol, phenylpyrrole, indoloxyl and 2-phenyl-5H-thiazole, does not reasonably provide enablement for compounds in which R³ is any arbitrary derivative of 1-naphthyl, phenylpyrrole, phenylthiophene, indole or 2-phenyl-5H-thiazole. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicants have not defined the meaning of the word "derivative". The Examiner therefore takes this term to encompass any substituent group including complex organic molecules. It is clear that Applicants' disclosure does not enable the synthesis of compounds in which the "derivatives" contain complex multifunctional substituent groups.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is "undue."

These factors include, but are not limited to:

- a. the breadth of the claims: In the instant case the claims are extremely broad encompassing compounds in which R^3 is any arbitrary derivative of 1-naphthyl, phenylpyrrole, phenylthiophene, indole or 2-phenyl-5H-thiazole.
- b. the nature of the invention: The instantly claimed invention is directed to novel compounds. The method for their manufacture is essential to the enablement of the invention. The compounds are intended for use as trypsin substrates and, as such, therefore acquire the low degree of predictability associated with predicting the structure of suitable enzyme substrates.
- c. the state of the prior art: the state of the prior art is generally considered high but would not allow one to predict in advance, based on Applicants' disclosure, which of the variety of possible reaction pathways, conditions and isolation/purification techniques, or combinations thereof, could be used to successfully manufacture any arbitrary derivative of 1-naphthyl, phenylpyrrole, phenylthiophene, indole or 2-phenyl-5H-thiazole.
- e. the amount of direction provided by the inventor: The inventors provide direction for the production of compounds in which R^3 is 1-naphthol, phenylpyrrole, indoloxyl and 2-phenyl-5H-thiazole only. No direction, or definition, is provided for any other derivatives. No specific guidance is provided with regard to determining which other derivatives would be suitable for the purposes of the invention.

f. the existence of working examples: The only working examples provided are directed to the production of compounds in which R³ is 1-naphthol, phenylpyrrole, indoloxo and 2-phenyl-5H-thiazole only. No direction, or definition, is provided to guide the selection and manufacture of any other derivative.

Based upon the analysis above, the broad range of claimed structures and the low degree of predictability associated with predicting enzyme substrates, the Examiner concludes that undue experimentation is required to make and use the invention as claimed.

10. Claim 1-5, 11, 42 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claims 1 (lines 5, 6 (twice), 7 (twice)) and 42 (lines 8, 9) recite the limitation "derivatives thereof". The meaning of the term "derivatives" has not been defined. It is therefore impossible to determine the intended scope of claims 1, 42 and their dependents. Claims 1, 42 and their dependents are therefore rendered indefinite.

Claim Objections

11. Claim 44 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

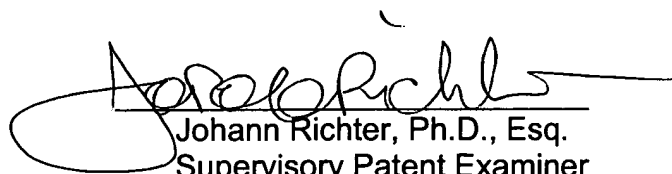
12. Claims 1-5 and 12 -44 are pending. Claims 1-5, 42 and 43 are rejected. Claim 44 is objected to. Claims 12 -41 are held withdrawn from consideration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

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